



# **Armed Forces College of Medicine AFCM**



# Mycobacteria

# Intended Learning Objectives (ILOs)

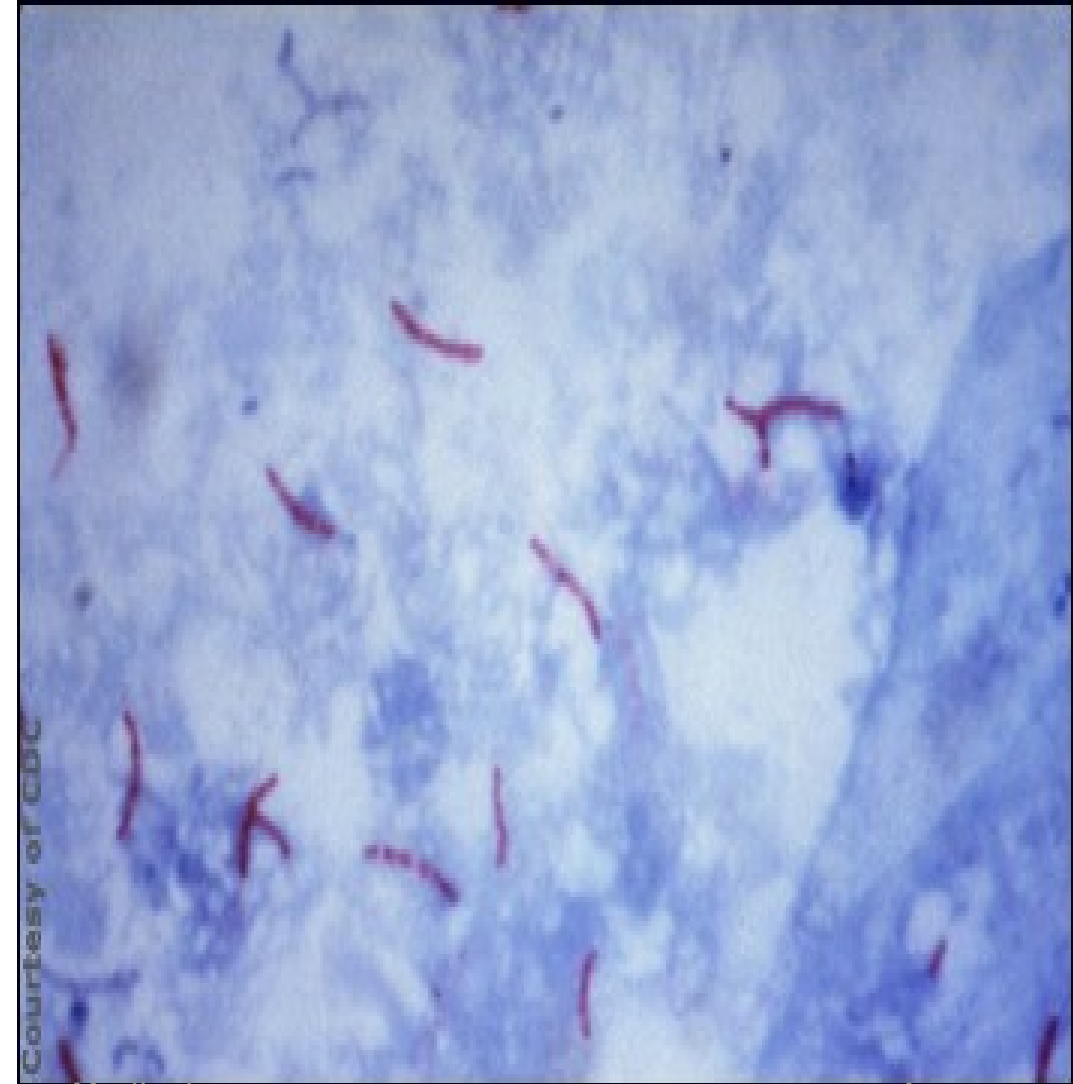
**By the end of this lecture the student will be able to:**

- Describe pathogenesis & clinical manifestations of pulmonary TB**
- Outline the laboratory diagnosis of pulmonary T.B.**
- Outline prevention and control of pulmonary T.B.**

# Mycobacteria



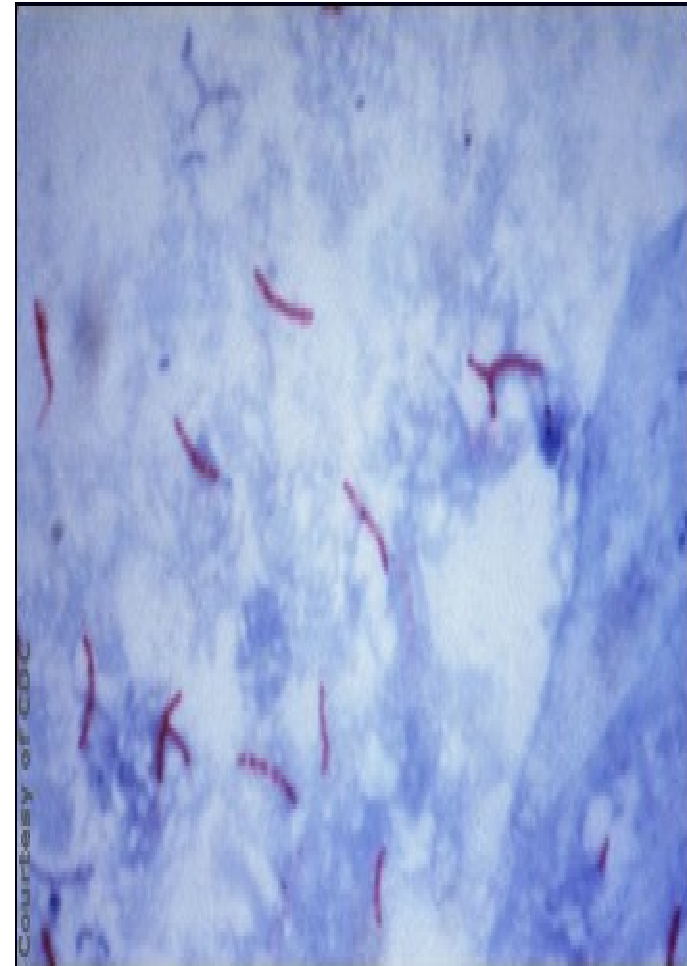
**Mycobacteria** are **aerobic** bacilli that have an unusual cell wall, resulting in their inability to be Gram-stained.



# Mycobacteria



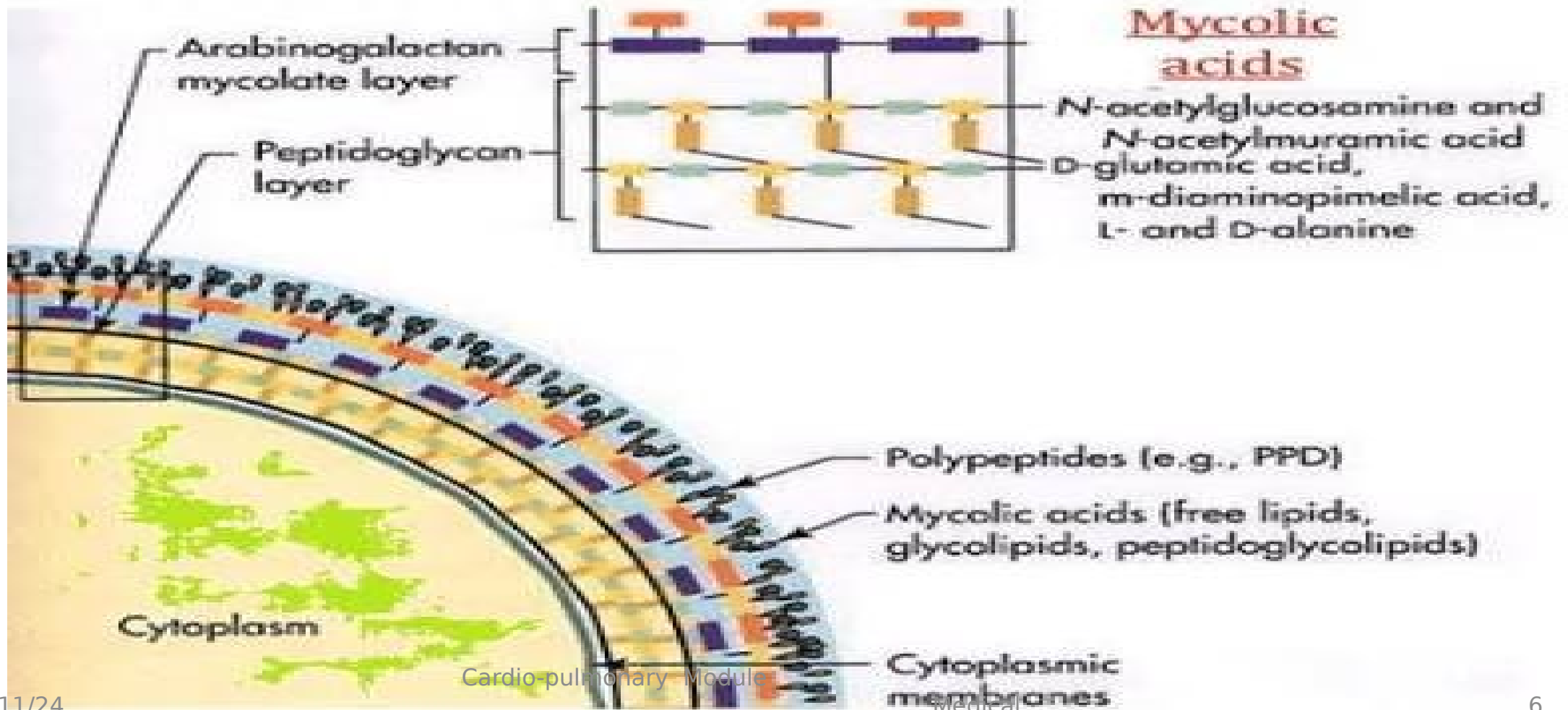
These bacteria are **ACID FAST** because they resist decolorization with acid/alcohol after being stained with carbol fuchsin. This is due to the high concentration of lipids, **mycolic acids**, in their cell wall



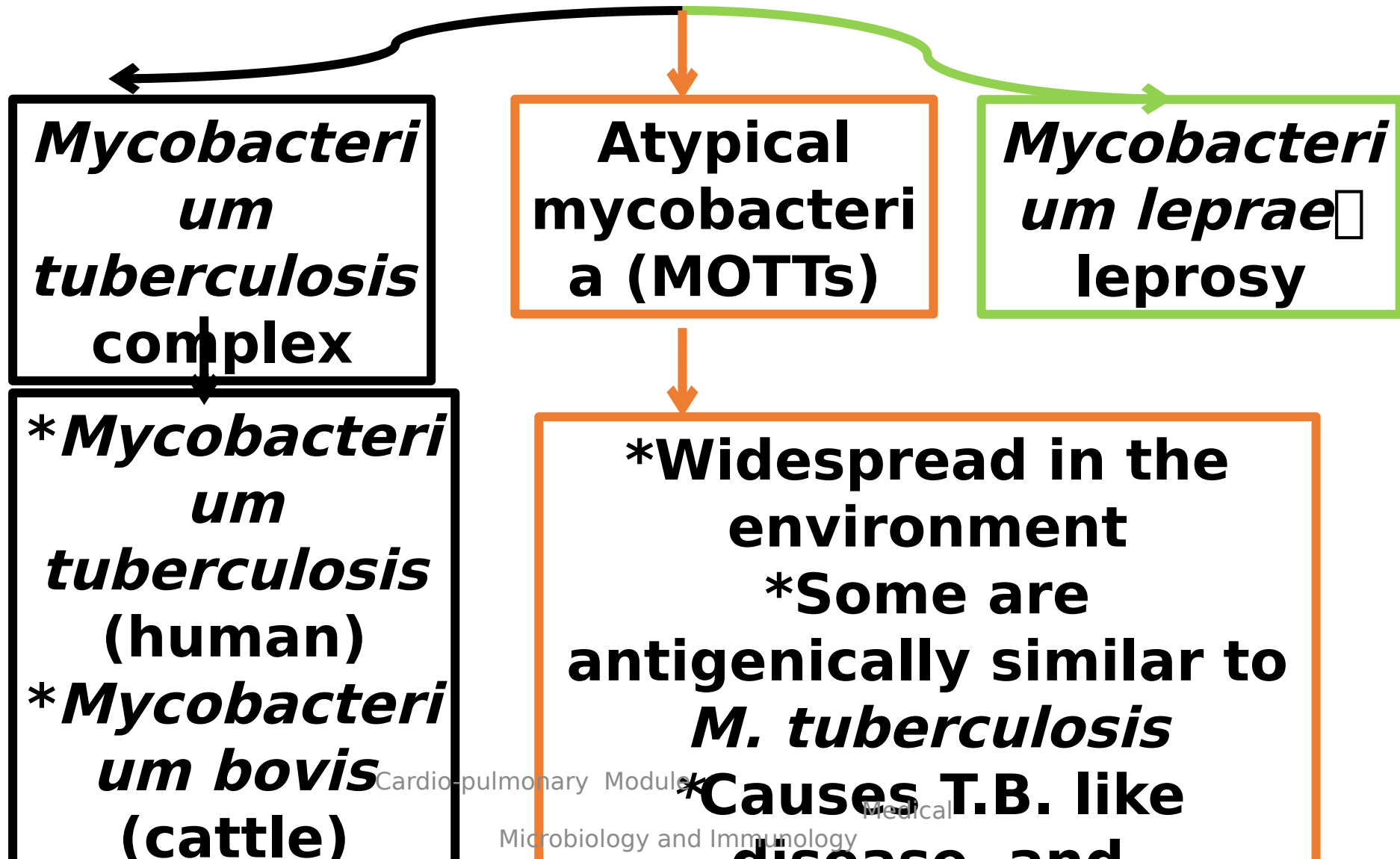
# Cell wall of Mycobacteria



## Lipid-Rich Cell Wall of Mycobacterium



# Members of Mycobacteria



# *Mycobacterium tuberculosis*- Disease

- This organism causes tuberculosis.
- Worldwide, *M. tuberculosis* causes more **deaths** than any other single microbial agent.
- One-third of the world's population is infected with this organism



# *Mycobacterium tuberculosis*- Properties



- *M. tuberculosis* is an **obligate aerobe** disease in highly oxygenated tissues (upper lobe of the lung and the kidney)
- Non motile non-capsulated and non-spore forming

# *Mycobacterium tuberculosis*- Properties

- Resistant to dehydration □ survives in dried expectorated sputum

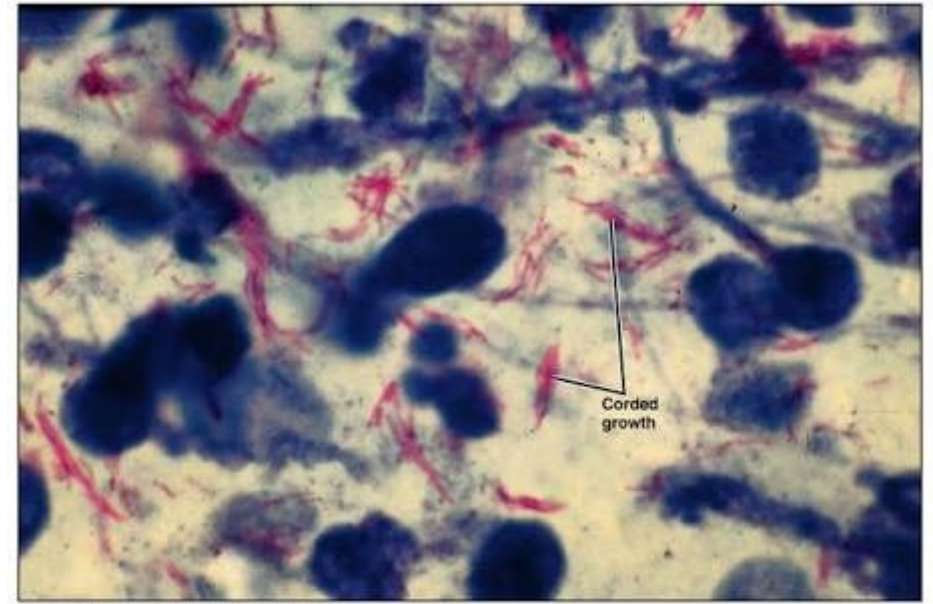
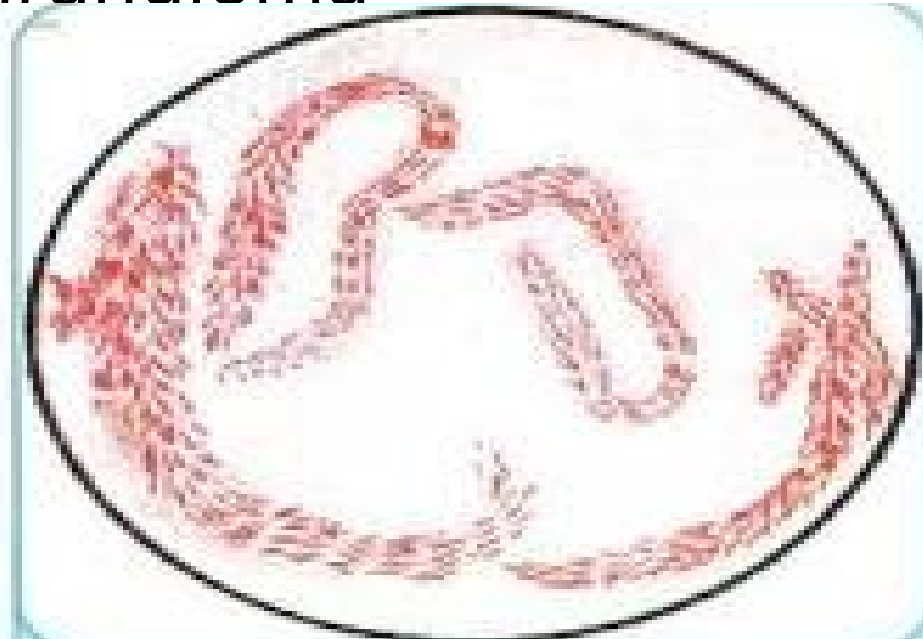
• **Grows slowly**

**Cultures incubated  
for 6 to 8 weeks  
before recording as  
negative**

**Prolonged  
course of  
TTT**

# *Mycobacterium tuberculosis*- Virulence factors

**1- Cord factor (glycolipid):** Virulent strains grow in a characteristic “serpentine” cordlike pattern, as the bacilli stick together □ toxic to leukocytes+ antichemotactic+ development of granuloma



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# ***Mycobacterium tuberculosis*- Virulence factors**



**2- Several antigenic proteins** □ elicit hypersensitivity reactions

**3- Mycolic acid:** inhibits formation of phagolysosome in macrophage → *INTRACELLULAR SURVIVAL*.

**4- Metabolically inactive:** difficult to kill by antibiotics

**5- Antibiotic resistance:** acquired by **chromosomal gene mutation.**

# *Mycobacterium tuberculosis*- Transmission



## *Mycobacterium tuberculosis*

- Person to person by respiratory **AEROSOLS** (mostly from smear positive patients) □ Lung □ reside in MQ.
- Humans are natural reservoir

## *Mycobacterium bovis*

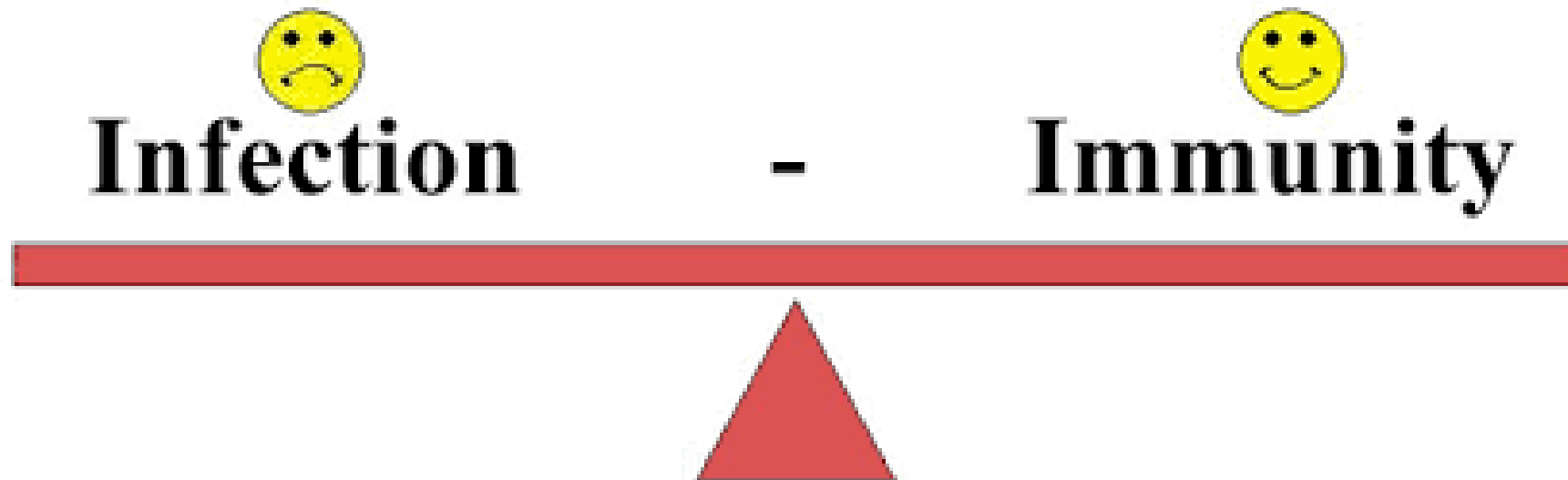
- Ingestion of unpasteurized milk from infected cows □ intestinal tuberculosis

**Risk factors: Immune suppression, poor housing, poor nutrition**

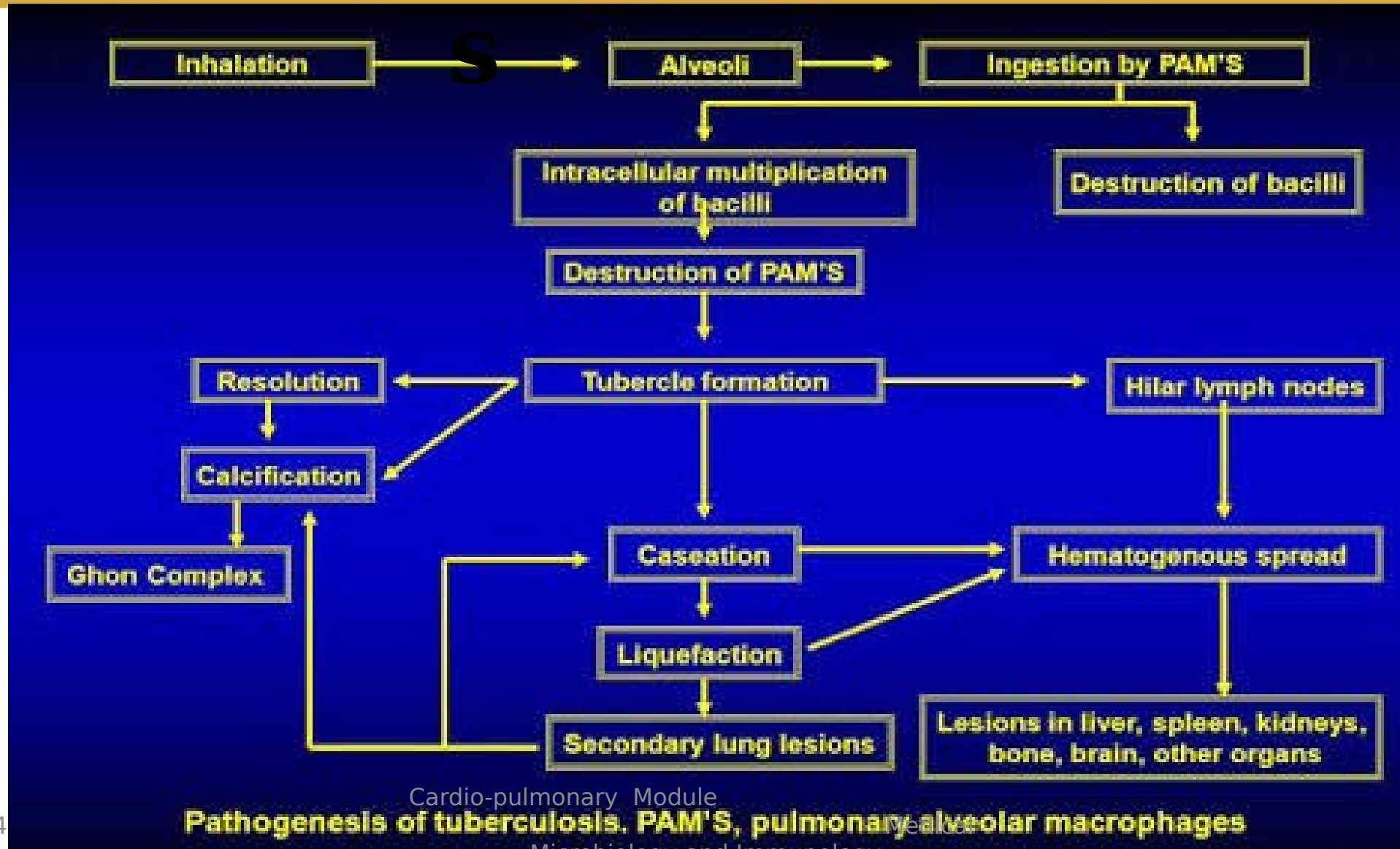
# Pathogenesis



- **NO** exotoxin... **NO** endotoxin
- MQ infection → phagosome → mycolic acid inhibits its fusion with lysosomes → the organism escapes the degrading lysosomal enzymes → Intracellular survival.



# Pathogenesis



Cardio-pulmonary Module  
**Pathogenesis of tuberculosis. PAM'S, pulmonary alveolar macrophages**

# Pathogenesis



Spread of the organism within the body occurs by two ways:

←  
**Tubercle erodes into a bronchus, empties its caseous contents, spread of the organism to other parts of the lungs, to the GIT if swallowed, and to other persons if expectorated**

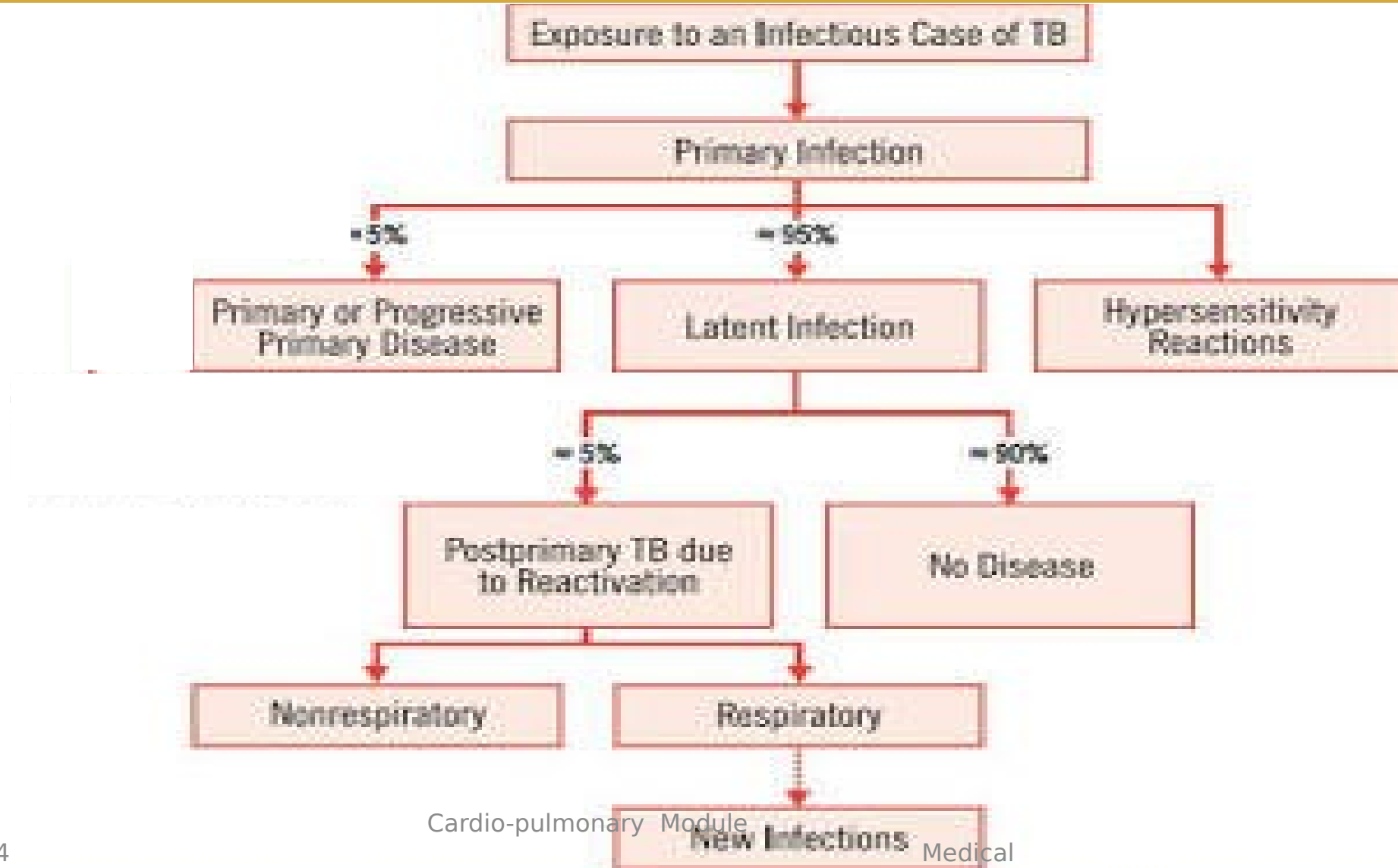
→  
**Via the bloodstream to many internal organs if cell-mediated immunity fails to contain the initial infection or at a late stage if a person becomes immuno-compromised**



# Immunity and Hypersensitivity

- After recovery from the primary infection, resistance to the organism is mediated by **Th-1**
- Circulating antibodies also form. Do they have a role in resistance??

# Clinical findings



# Clinical findings



- **Asymptomatic: Latent infection...**
- **Generally: fever, night sweating, weight loss**
- **Pulmonary: cough, expectoration.. Hemoptysis??**
- **Extrapulmonary: lymphadenitis (most common), erythema nodosum**

# Clinical findings



- **GIT:** abdominal pain and diarrhea, intestinal obstruction or hemorrhage may occur.
- **Oropharyngeal tuberculosis:** painless ulcer + lymphadenopathy

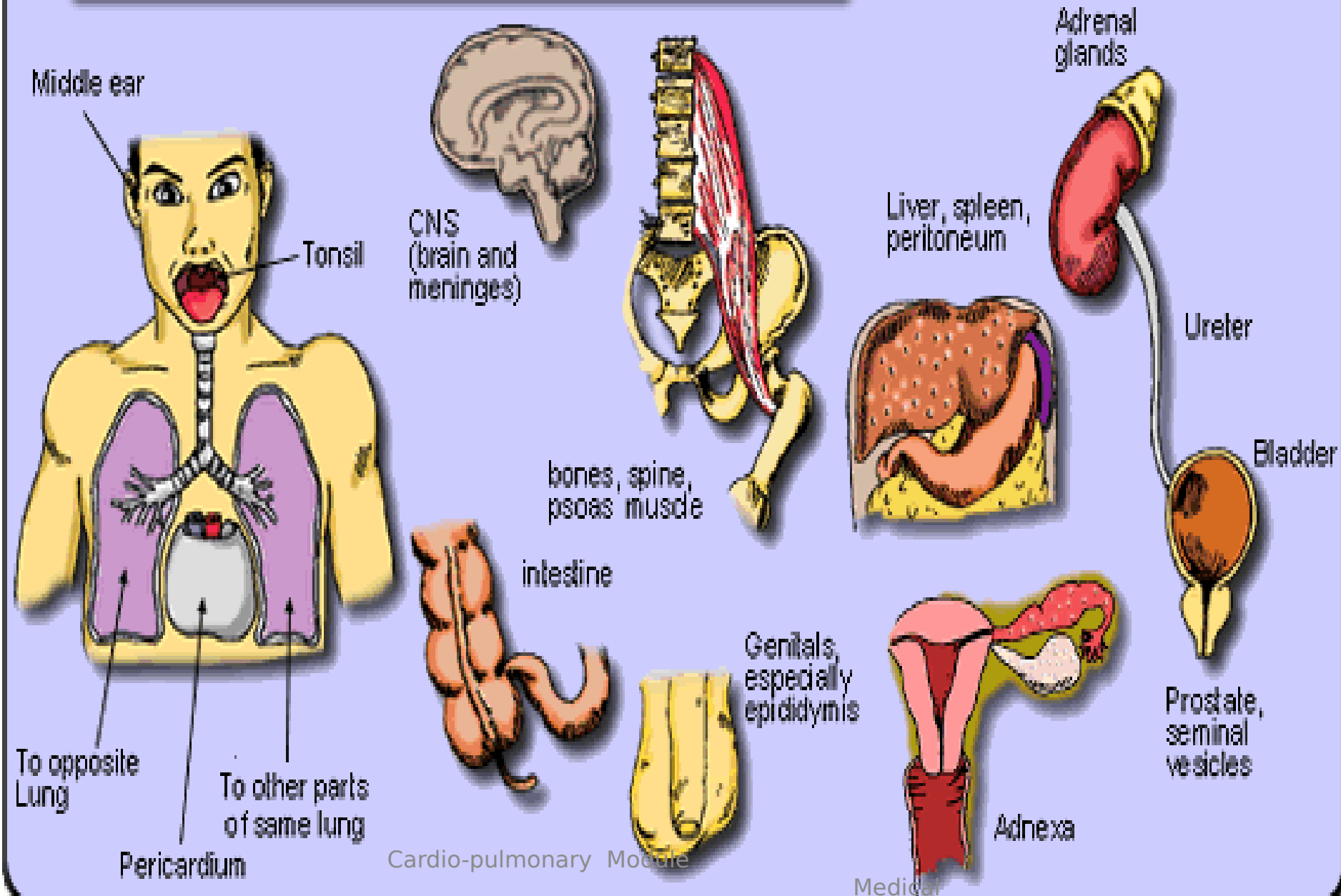
# Clinical findings



- **Renal tuberculosis:** mostly reactivation lesion □ dysuria, hematuria, and flank pain occur. **“Sterile pyuria”** is a characteristic finding???
  - **Miliary T.B.:** multiple disseminated lesions resembling millet seeds
- **Tuberculous meningitis**  
and **tuberculous osteomyelitis**,  
specially vertebral osteomyelitis  
(Pott’s disease), are important disseminated forms.



# Tuberculosis Affects Many Parts of the Body



# Laboratory Diagnosis



1- **Acid fast staining** of sputum or other specimens by **ZN** stain

2- **Isolation and identification:** culture is performed on **L.J.** medium□ incubated for up to **8 weeks**

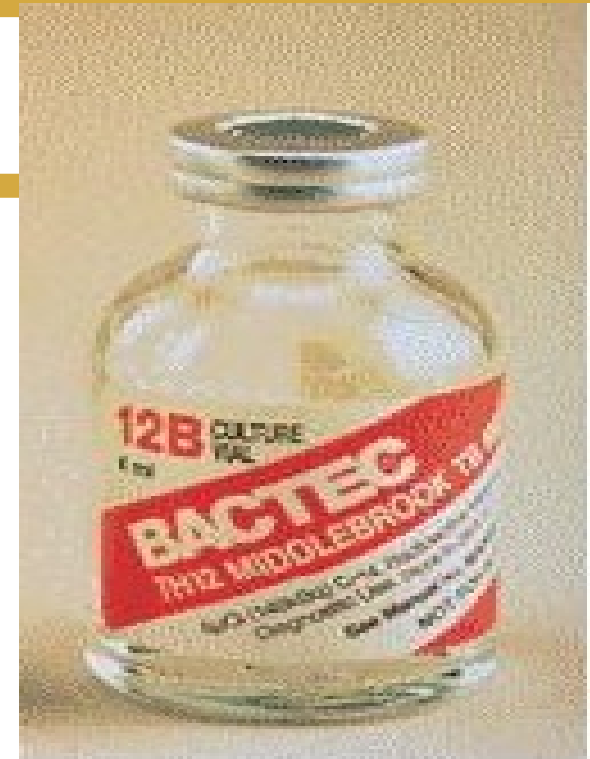
- In liquid BACTEC medium, radioactive metabolites are present, and growth can be detected by the production of radioactive carbon dioxide in about **2 weeks.**

**OBSOLETE**

3- **PCR and nucleic acid amplification techniques:** detect the presence of *M. tuberculosis* directly in clinical specimens



**Specimen containing TB**

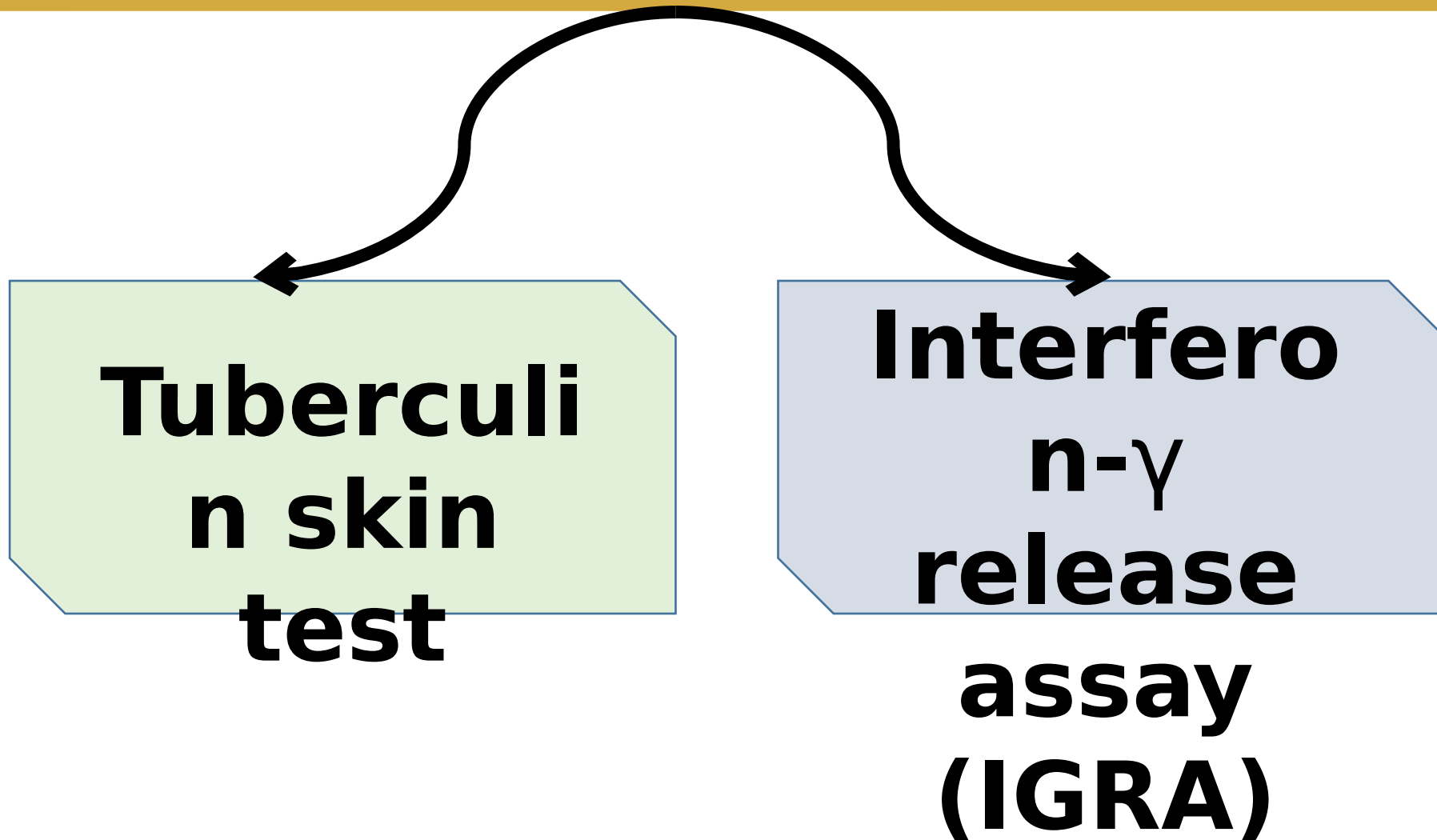


**Utilize <sup>14</sup>C labeled palmitic as  
a single carbon source**

**Radioactive  
CO<sub>2</sub>**



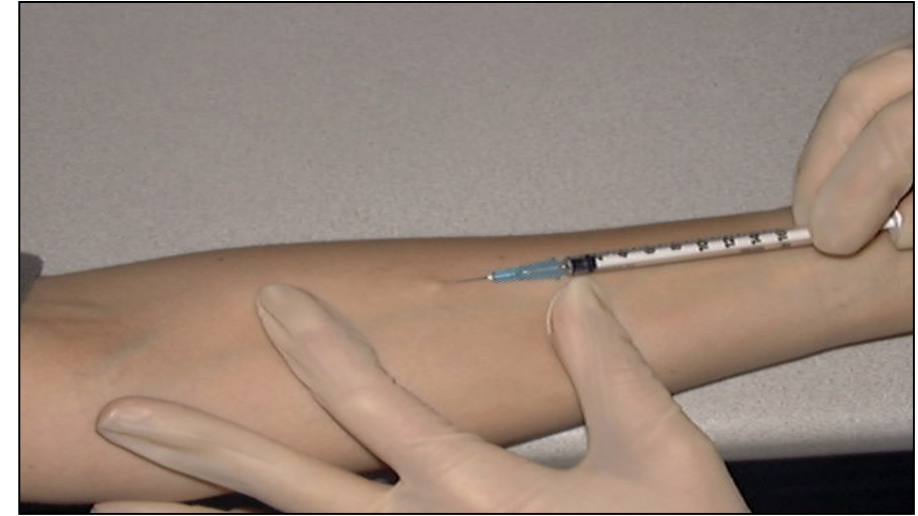
# Laboratory Diagnosis of Latent T.B.



# Tuberculin skin test



Purified protein derivative  
**(PPD)** is the antigen used  
injected intra-dermally  
delayed hypersensitivity  
reaction within 72 hours  
induration surrounding the test  
site measuring its diameter  
which depends on the status of  
the individual being tested



# Tuberculin skin test



- The test is considered **positive** when the diameter is:

## 15 mm or more

- In a person who has no known risk factors

## 10 mm or more

- In a person with high-risk factors, (homeless person, intravenous drug users, medical staff.

## 5 mm or more

- In a person who has deficient cell-mediated immunity (e.g. AIDS patients) or close contact with a person with active tuberculosis

# Tuberculin skin test



- **A positive skin test result indicates previous exposure to the organism but not necessarily active disease.**
- The tuberculin test becomes positive 4 to 6 weeks after infection

# Interferon- $\gamma$ release assay (IGRA)

**Blood cells from the patient are exposed to antigens from *M. tuberculosis* (in**

**\*\*This antigen is NOT PRESENT in BCG**



**Amount of interferon- $\gamma$  released from the cells is measured**

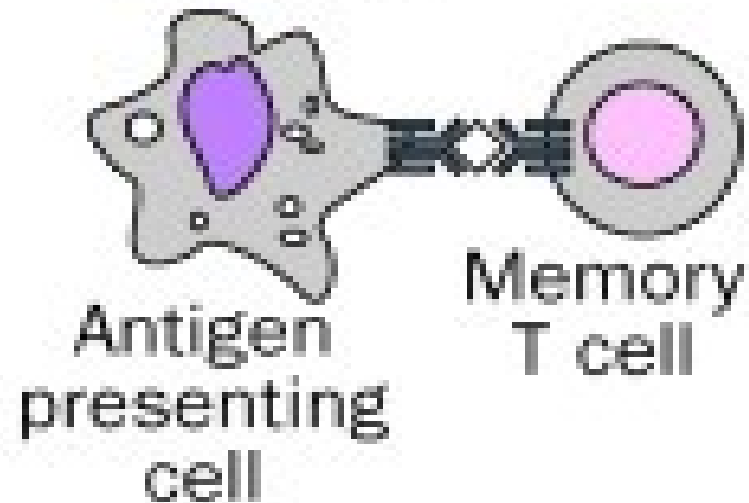
**Advantages??**

Cardio-pulmonary Module

Medical

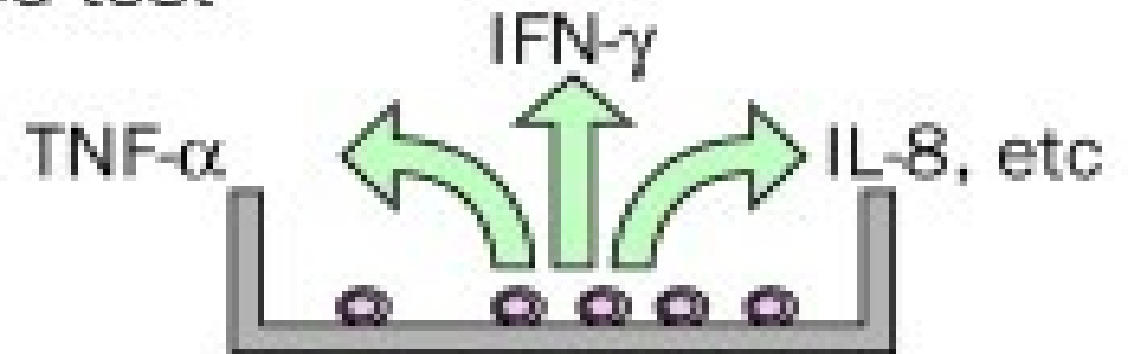
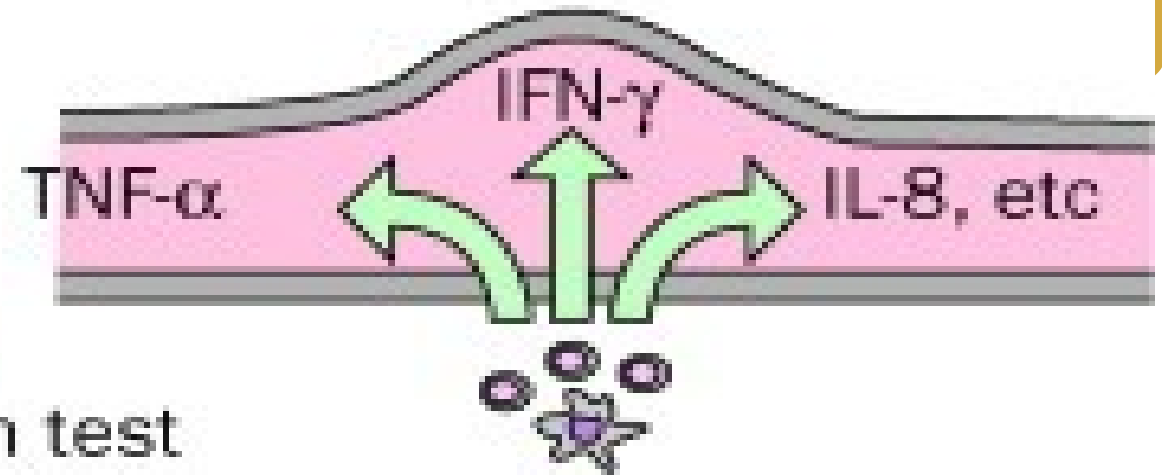
# Measurement of induration and erythema

## Presentation of mycobacterial antigens



↗ Skin test

↘ in-vitro blood test



## Measurement of IFN- $\gamma$ production

# Emergence of T.B.



- **Tuberculosis emerging today as a leading infectious killer of youth and adult all over the world:**

1- Increased incidence of HIV infection.

2- Emergence of MDR strains.

3- —————→



# Prevention of T.B.



**1- BCG vaccine:** induces partial resistance to tuberculosis. **Does not** prevent disease. Prevents mortality in children under 5 years of age.

The vaccine contains a strain of **live-attenuated** *M. bovis* called **B**acillus Calmette-**G**uérin.

- Effectiveness ranges from 0% to 70%.





**2- Pasteurization of milk prevents intestinal T.B.**

**3- To prevent spread to medical personnel, other patients and the environment: Airborne isolation precautions**

**4- Tuberculin skin test to detect recent converters in: people with HIV infection, close contacts of patients with active tuberculosis, alcoholics and intravenous drug users, HCWs exposed to patients**